IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) [redacted]
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC. Plaintiff/Counter-Defendants.	REDACTED - PUBLIC VERSION

SAREPTA THERAPEUTICS, INC. AND THE UNIVERSITY OF WESTERN AUSTRALIA'S OPPOSITION TO NIPPON SHINYAKU CO., LTD. AND NS PHARMA, INC.'S MOTION TO EXCLUDE OPINIONS OF DR. STEVEN DOWDY, PH.D.

I. INTRODUCTION

NS bases its motion to exclude post-priority evidence on a fundamentally flawed premise. NS argues that "Dr. Dowdy's supplemental opinions go far beyond Sarepta's representation" that the evidence at issue "illuminat[es] the state of the art as of the priority date." D.I. 613 at 1. Not so. There is no new post-priority evidence in Dr. Dowdy's supplemental opinions, nor are there new opinions characterizing the evidence differently than before or conceding that the evidence is irrelevant. Instead, NS's present motion is a rehash of its prior motion in limine, which the Court already denied. D.I. 536-15; D.I. 570 (Pre-Trial Conference Tr.) at 11:16-25. On that basis alone, the Court should deny this motion. In any event, NS's motion to exclude evidence of written description (not enablement) lacks merit. Sarepta's patent structurally defines a small group of ASOs that induce exon 53-skipping. Sarepta's post-priority evidence demonstrates that ***every*** ASO made according to the teachings of Sarepta's patent – including ASOs made by NS for purposes of this litigation – induced exon 53-skipping. Such evidence illuminates the state of the art as of the priority date, because it confirms that the disclosed and claimed ASOs consistently perform as expected. As with NS's prior motion in limine directed to the same exact evidence, the Court should deny this motion in its entirety.

II. ARGUMENT

There is no dispute that post-priority evidence is properly before the jury for ***enablement***.[1] NS only challenges the use of post-priority evidence to confirm "a structure-function correlation,"

[1] *See, e.g.*, *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1379 (Fed. Cir. 2017) (*Amgen I*) (post-priority evidence "may show, for example, that practicing the invention did not require undue experimentation [*i.e.*, enablement] . . ."); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1336 (Fed. Cir. 2003) ("[N]umerous post-filing publications . . . demonstrated the extent of the enabling disclosure.").

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i.e., ***written description*** of ASO structure/sequence correlated with exon 53-skipping.[2] *See* D.I. 613; D.I. 613-2. NS claims that Dr. Dowdy's supplemental opinions are inconsistent with a prior representation by Sarepta, namely that the evidence at issue "illuminat[es] the state of the art as of the priority date." D.I. 613 at 1. That is wrong. To be clear, there is no new post-priority evidence in Dr. Dowdy's supplemental opinions, and NS does not identify any. Nor does NS explain how Dr. Dowdy relies on the evidence differently than before. To the extent NS suggests Dr. Dowdy agreed post-priority data necessarily "would not reflect the understanding of a POSA" as of the priority date (D.I. 613 at 1, 4 n.3), that is not the case. Dr. Dowdy testified only that one particular post-priority reference regarding a different exon (43) – and proffered by ***NS's*** expert, Dr. Hastings – was irrelevant to the exon 53 hotspot. Ex. 1 (Dowdy Supp. Tr.) at 363:25-364:9 (referring to the "[t]he data relating to exon 43").

This motion is nothing more than a do-over of NS's prior motion in limine. *See* D.I. 536-15. In the current motion, just like the last one, NS asks the Court to categorically exclude the wealth of evidence ***confirming*** that the claimed ASOs induce exon 53-skipping. *Compare* D.I. 536-15 at 1 ("Such reliance on the post-priority date art to ***'confirm'*** written description, enablement, and supposed predictability is barred by Federal Circuit law.") *with* D.I. 613 at 1 ("The Court should therefore exclude Dr. Dowdy's opinions relying on later-discovered species as supposedly ***'confirming'*** a structure-function correlation . . ."). As Sarepta explained in

[2] NS mentions the word "enablement" only twice, neither one relating to its current post-priority evidence arguments. The first instance describes in passing NS's ***prior*** motion. D.I. 613 at 1. ("When NS moved in limine to bar Sarepta's reliance on post-priority date art to support written description and enablement . . ."). The second instance (inaptly) quotes from *Idenix Pharms. LLC v. Gilead Scis. Inc.* for the proposition that "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention." D.I. 613 at 1 (citing 941 F.3d 1149, 1159 (Fed. Cir. 2019)). But that language has nothing to do with post-priority evidence.

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response to NS's prior motion, post-priority evidence is appropriate to support written description.[3] The Court, after considering the parties' briefing and hearing oral argument, denied NS's prior motion. D.I. 570 (Pre-Trial Conference Tr.) at 11:16-25 ("So on MIL No. 1, to the extent it requests a blanket exclusion of post-priority date evidence, that request will be denied."). The Court should deny NS's current motion for that reason alone.

NS's motion fails on the merits as well. NS argues that the patent does not sufficiently describe the claimed genus of ASOs, because "there is at most only 'one representative species' disclosed in the specification and [redacted] and "none of the exon 53 ASOs disclosed in the specification have been tested in clinical trials." D.I. 613 at 2-3. But a patentee is not required to exemplify or reduce to practice every species of a genus, much less use them in clinical trials. *Alcon Rsch. Ltd. V. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1191 (Fed. Cir. 2014) (written description "is not about whether the patentee has proven to the skilled reader that the invention works"); *United Therapeutics Corp. v. Liquidia Techs, Inc.*, 74 F.4th 1360, 1371 (Fed. Cir. 2023) ("Again, because safety and efficacy are not recited in the claims, we need not deal with Liquidia's [written description] arguments.").

Here, Sarepta's patent discloses and claims a genus of ASOs targeting a newly-discovered "hotspot" region that spans only 47 nucleotides (out of the millions of nucleotides in the dystrophin gene and the 212 nucleotides of exon 53). D.I. 427-1, Ex. 1 (Dowdy Op. Rep.) at ¶ 74; D.I. 612-1, Ex. 4 (Hastings Supp. Expert Rep.) at ¶ 50. Those ASOs also have a specific length (20-31 nucleotides) and chemistry (PMO), at least 12 consecutive bases of SEQ ID No: 195, and "100%

[3] *Amgen I*, 872 F.3d at 1379 (post-priority evidence "may show, for example, . . . that the disclosed species are representative of the claimed genus [*i.e.*, written description])"; *Amgen Inc. v. Sanofi*, C.A. No. 14-1317-RGA, 2019 WL 11071409, at *2-3 (D. Del. Feb. 14, 2019) (*Amgen II*) (allowing post-priority evidence that "illuminates the state of the art at the priority date").

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complementarity to consecutive bases of a target region of exon 53 throughout the entire length of the [ASO]." Ex. 2 (Dowdy Supp. Reb. Rep.) at ¶¶ 15-17, 62, 103-104; D.I. 427-2, Ex. 2 (Dowdy Reb. Rep.) at ¶ 74; D.I. 573. Accordingly, Sarepta's patent structurally defines the claimed genus of ASOs, including a specific and finite number of sequences (168). Dr. Dowdy has reviewed the teachings in the patent, including the examples of ASOs targeting exon 53, and concludes "a POSA would have understood that most, if not all, candidate ASOs [*i.e.*, with the 168 possible ASO sequences] would induce exon 53 skipping because they are directed to the exon 53 hot spot disclosed" in Sarepta's patent.[4] Ex. 2 (Dowdy Supp. Reb. Rep.) at ¶ 135.

Dr. Dowdy properly relies on post-priority evidence showing that ASOs chosen from the 168-sequence genus dependably induce exon 53-skipping, consistent with the teaching of the patent. Ex. 2 (Dowdy Supp. Reb. Rep.) at ¶ 126; D.I. 427-2, Ex. 2 (Dowdy Reb. Rep.) at ¶ 92. Because Sarepta's patent itself defines the structure of all claimed exon 53-skipping ASOs, Dr. Dowdy is not relying on "later-discovered species that have (1) different base sequences; (2) a different backbone chemistry (morpholino); and (3) different levels of functional activity than the exon 53 ASOs disclosed in the specification." D.I. 613 at 3-4 (emphasis omitted). Indeed, NS and its expert, Dr. Hastings, [redacted]

Ex. 2 (Dowdy Supp. Reb. Rep.) at ¶ 128. Far from implicating "later-discovered species" or other

[4] NS argues that "Dr. Dowdy concedes that testing is required to determine whether an ASO meeting the structural criteria (a candidate) will meet the claim's functional requirement." D.I. 613 at 2. Dr. Dowdy made no such concession. He has consistently taken the position that "there is a high probability that . . . [a]ny oligo that fulfills the criterion in claim 1 that the POSA would see, would induce exon 53 skipping." Ex. 1 (Dowdy Supp. Tr.) at 258:23-259:4; *see also* D.I. 427-13 (Dowdy Tr.) at 44:11-15 ("The expectation would be exon skipping."); Ex. 2 (Dowdy Supp. Reb. Rep.) at ¶ 18 (claimed "candidates" are "largely coextensive with the number of ASOs that induce exon 53 skipping").

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new inventions, the post-priority evidence in this case merely confirms the structure-function correlation that was already set forth in the patent. Although NS can cross-examine Dr. Dowdy on the post-priority evidence and its connection to the disclosure of the patent specification, it cannot exclude this evidence.

The cases that NS relies on are inapposite. D.I. 613 at 1-2. Those cases do not stand for excluding "after-the-fact functional testing" to confirm a patent's teachings. D.I. 613 at 3. Again, NS is itself relying on "after-the-fact functional testing" in this case. D.I. 612-1, Ex. 4 (Hastings Supp. Rep.) at ¶¶ 156-82. Those cases merely found that, when a patent does not describe an element of a claim in the first instance, a patentee cannot rely on new discoveries or developments to fill that gap. In *Juno*, the claims required CD19-specific single-chain antibody variable fragments (scFvs), and the realm of possible structures was "vast." *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1340 (Fed. Cir. 2021). The court held that there were very few known examples of CD19-specific scFvs as of the priority date, and the inventor's later screening of scFv sequences was irrelevant to written description. *Id.* at 1340-41. In *Biogen*, the claims required an effective dose of 480 mg/day. *Biogen Int'l GMBH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1337 (Fed. Cir. 2021). The court found that the patent did not describe that specific effective dose, "because the specification's only reference to [480 mg/day] was part of a wide DMF-dosage range and not listed as an independent therapeutically efficacious dose." *Id.* at 1343.

The situation here is different. As explained above, the specification discloses and claims a structurally-defined genus of ASOs, and a POSA would have expected those ASOs to induce exon skipping. Consistent with that disclosure, Sarepta's post-priority evidence shows that ***every*** ASO tested within the scope of Sarepta's patent claim – including ASOs that NS designed and tested for purposes of this litigation – induced exon 53-skipping as taught in the patent. *See, e.g.,*

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Ex. 2 (Dowdy Supp. Reb. Rep) at ¶ 18. Such evidence conclusively confirms that the inventors of Sarepta's patent were right, and is admissible for that purpose. *See, e.g.*, *Amgen II*, 2019 WL 11071409, at *2–3 (allowing post-priority evidence that "illuminates the state of the art at the priority date").

III. CONCLUSION

For the above reasons, the Court should deny NS's Motion to Exclude Opinions of Dr. Dowdy in its entirety.

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CERTIFICATE OF SERVICE

I hereby certify that on October 16, 2024, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on October 16, 2024, upon the following in the manner indicated:

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